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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,101	05/18/2001	Robert D. Mass	3118/1H146US1	9233

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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/863,101	MASS, ROBERT D.	
	Examiner	Art Unit	
	Anne Holleran	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21 and 26* is/are rejected.

7)☒ Claim(s) *25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/20/2005 & 11/9/2004
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed November 9, 2004 is acknowledged.

2. Claims 21, 25 and 26 are pending and examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Withdrawn:

4. The rejection of claim 25 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment.

5. The rejection of claims 21, 25 and 26 under 35 U.S.C. 103(a) as being unpatentable over Baselga I (Baselga, Journal of Cinical Oncology, 14: 737-744, 1996; cited in IDS) or Baselga II (Baselga, Semin. Oncol., 26(4): 87-83, 1999) in view of either Pauletti (previously identified as "Godolphin"; Oncogene, 13: 63-72, 1996; of record) or Persons (Annals of Clincial and Laboratory Science, 30: 41-48, 2000, Jan.; cited in IDS) is withdrawn in view of the amendment changing the scope of the claims to a method for treating patients that express HER2 at 0 or 1+

level by immunohistochemistry and also have a HER2 gene amplification. The prior art of record does not teach or fairly suggest claims with this limitation.

New Grounds of Rejection:

Claim Rejections - 35 USC § 112

6. Claims 21 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods where the HER2 antibody is huMAb4D5-8, does not reasonably provide enablement for methods for identifying and treating patients disposed to respond favorably to any HER2 antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The claimed inventions are drawn to methods for identifying and treating breast cancer patients disposed to respond favorably to a HER2 antibody, wherein the patient's tumor cells express HER2 at 0 or 1+ level by immunohistochemistry, comprising detecting HER2 gene amplification in tumor cells in a tissue sample from the patient and treating the patient with HER2 gene amplification. The basis for the claimed methods is that the specification provides

data showing that those patients having HER-2 amplification respond favorably to Herceptin when compared to patients who do not have a HER2 gene amplification.

The prior art has recognized that HER2 status is a predictor of response of response to Herceptin therapy and that HER2 status may be measured by detecting HER2 protein overexpression by immunohistochemical methods or by detection of HER2 gene amplification. The prior art favored the use of immunohistochemical methods for measuring HeR2 status, because the test was considered more practical in a clinical trial setting (Jacobs, J. Clinical Oncol, 17(7): 1974-1982, 1999). Currently, it is accepted that HER2 status should be assessed before beginning a treatment with Herceptin, and two methods that may be used are a measure of gene amplification by FISH or a measure of HER2 protein expression by immunohistochemistry with a HER-2 specific antibody (Nahta, Clinical Cancer Research, 9: 5078-5084, 2003; page 5078, 2nd col.). However, there are no teachings in the prior art demonstrating an association between HER2 status (either protein overexpression or gene amplification) and a favorable response to anti-HER2 antibodies other than Herceptin. Furthermore, the mechanism by which Herceptin causes regression of breast tumors is not completely understood (Nahta, Clinical Cancer Research, 9, 5078-5084; page 5079). Also, there appears to be some anti-HER2 antibodies (e.g. 2C4) that are effective on breast tumors that express normal levels of HER2 and do not overexpress HER2 (Nahta, Clinical Cancer Research, 9, 5078-5084; page 5080).

The specification provides data that demonstrates that favorable response to Herceptin is linked to HER2 gene amplification, and fails to demonstrate such a correlation between a response to any other anti-HER2 antibody and HER2 gene amplification. The prior art also fails to demonstration an association between favorable outcome with any other anti-HER2 antibody

and HER2 gene amplification. Thus, to practice the full scope of the claimed inventions further experimentation would have to be done by a skilled worker to discover if an association exists between favorable response to treatment with an anti-HER2 antibody and gene amplification. This further experimentation is undue experimentation because it is unpredictable whether such an association would be discovered. Therefore, the specification presents an invitation for further experimentation, where the outcome of the further experimentation is not predictable. This is in contrast to the situation in Wands (858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)), where the outcome of the further experimentation was predictable, i.e. that someone in possession of a protein would be able to make a monoclonal antibody to that protein.

Because of the narrow scope of the teachings of the specification, where the specification is directed to demonstrating an association between gene amplification and response to Herceptin therapy, and because the prior art fails to show that an association between gene amplification and response to any other anti-HER2 antibody, and because the discovery of such an association is unpredictable for other anti-HER2 antibodies, the full scope of the claims, where the claims are directed to identifying and treating a patient disposed to respond favorably to any anti-HER2 antibody, is not enabled by the specification.

Conclusion

No claim is allowed. Claim 25 is objected to for depending from a rejected claim.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran
Patent Examiner
March 9, 2005

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER
03/11/2005